

Remarks

I. Support for the Amendments

The amendments to the specification are sought to correct several inadvertent typographical errors, including one in the deposit number of a previously deposited recombinant host. Support for the amendment correcting the deposit number can be found in the present specification at page 59, lines 1-4. The amendments to claim 66 are sought to correct minor and inadvertent typographical errors. Hence, these amendments do not add new matter and their entry and consideration are respectfully requested.

II. Status of the Claims

Claims 1, 2, 5-33, 66, and 69-72 are pending in the application, with claims 1, 2, 23 and 66 being the independent claims.

III. Summary of the Office Action

In the Office Action dated February 26, 2003, the Examiner has made two rejections of, and one objection to, the claims. Applicants respectfully request that the Examiner reconsider all outstanding rejections and objections and that they be withdrawn.

IV. The Rejection Under 35 U.S.C. § 103(a) Over Caetano-Anolles

In the Office Action at pages 3-4, the Examiner has rejected claims 1, 2, 5-6, 9-15, 23-29 and 66 under 35 U.S.C. § 103(a), as being unpatentable over Caetano-Anolles, *et al.*

(WO 95/33853, Document A cited on Form PTO-892 attached to paper No. 10, hereinafter "Caetano-Anolles"). Applicants respectfully traverse this rejection.

Present claim 1 (and hence, claims 5, 6 and 9-15 that depend ultimately therefrom and that are also rejected) recites a method of identifying, analyzing or typing a polymorphic DNA fragment in a sample of DNA, comprising contacting the sample of DNA with one or more DNA polymerases, wherein the DNA polymerases are mutated to be substantially reduced in the ability to add one or more non-templated nucleotides to the 3' terminus of a DNA molecule; amplifying the polymorphic DNA fragment within the sample; and analyzing the amplified polymorphic DNA fragment.

Present claim 2 recites a method of producing amplified copies of a polymorphic DNA fragment which comprise substantially no non-templated 3' terminal nucleotides, comprising contacting a DNA sample with one or more DNA polymerases, wherein the DNA polymerases are mutated to be substantially reduced in the ability to add one or more non-templated nucleotides to the 3' terminus of a DNA molecule; and amplifying the polymorphic DNA fragment within the DNA sample.

Present claim 23 (and hence, claims 24-29 that depend ultimately therefrom and that are also rejected) recites a kit comprising one or more DNA polymerases, wherein the DNA polymerases are mutated to be substantially reduced in the ability to add one or more non-templated nucleotides to the 3' terminus of a DNA molecule.

Present claim 66 recites: A method for amplifying a double stranded DNA molecule, comprising: (a) providing a first and second primer, wherein the first primer is complementary to a sequence at or near the 3'-terminus of the first strand of the DNA

molecule and the second primer is complementary to a sequence at or near the 3'-terminus of the second strand of the DNA molecule; (b) hybridizing the first primer to the first strand and the second primer to the second strand in the presence of the one or more DNA polymerases which have been mutated to reduce, substantially reduce or eliminate the ability of the polymerases to add non-templated 3' nucleotides to a synthesized nucleic acid molecule under conditions such that a third DNA molecule complementary to the first strand and a fourth DNA molecule complementary to the second strand are synthesized; (c) denaturing the first and third strands, and the second and fourth strands; and (d) repeating steps (a) to (c) one or more times.

A common recitation in these four independent claims of the present invention is the use of DNA polymerases which have been mutated to at least substantially reduce their ability to add one or more non-templated nucleotides to the 3' terminus of a DNA molecule.

The Examiner contends that Caetano-Anolles discloses a method of DNA fingerprinting which utilizes a DNA polymerase which does not have associated 3'-5' or 5'-3' exonuclease activity. However, Caetano-Anolles clearly does not disclose the use of a DNA polymerase that has been mutated to at least substantially reduce its ability to add one or more non-templated nucleotides to the 3' terminus of a DNA molecule. Indeed, the Examiner acknowledges this deficiency in Caetano-Anolles (*see* Office Action at page 3, section 7, third paragraph). However, the Examiner does not provide any disclosure, either from Caetano-Anolles, or from any other reference, that would cure this deficiency.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re*

Piasecki, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). In the present case, this burden has not been met -- by the Examiner's own acknowledgment, Caetano-Annoles provides no objective teaching that would have led one of ordinary skill to make and use a DNA polymerase mutated to at least substantially reduce the ability of the polymerase to add one or more non-templated nucleotides to the 3' terminus of a DNA molecule. Therefore, under *Piasecki* and *Fine*, this reference alone cannot be used as the basis for a *prima facie* case of obviousness of the presently claimed invention.

Apparently recognizing the deficiencies in Caetano-Annoles, the Examiner attempts to cure these deficiencies by pointing to the definition of "DNA polymerases" that is contained in Applicants' own specification. *See* Office Action at page 3, section 7, fourth paragraph. This approach is legally improper. The Examiner is respectfully reminded that a *prima facie* case of obviousness *cannot* be based whatsoever on an Applicants' own disclosure. *See In re Pleuddemann*, 910 F.2d 823, 828 (Fed. Cir. 1990) (noting that use of an applicant's specification as though it were prior art to support an obviousness determination is legal error); *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991) (holding that the evidence required to support a *prima facie* case of obviousness "must be founded in the prior art, not in the applicant's disclosure."). Thus, the attempt to fill the deficiencies in Caetano-Annoles using a definition of "DNA polymerases" that is contained in the present

specification is legally impermissible, and cannot be used to attempt to establish a *prima facie* case of obviousness in the present case.

Applicants also note that in making this rejection, the Examiner may be contending that based on the definition of "DNA polymerases" in Applicants' specification, the DNA polymerase disclosed in Caetano-Annoles may *inherently* be reduced in the ability to add one or more non-templated nucleotides to the 3' terminus of a DNA molecule. This contention is also without merit, for at least two reasons. First, as noted above, Applicants' specification cannot be used to fill the deficiencies in the cited art. Second, Applicants remind the Examiner that there is no such thing as "inherent obviousness," since inherence and obviousness are different legal concepts. *See In re Spormann*, 150 USPQ 449, 452 (C.C.P.A. 1966). That which is inherent cannot be obvious, since inherent information "is not necessarily known . . . [and] Obviousness cannot be predicated on what is unknown."

Id. Since the present rejection is based on obviousness, any contention by the Examiner that is based on the possible presence of inherent knowledge in *any* source (let alone in Applicants' own disclosure, which also cannot be used for the reasons noted above) must necessarily fail.

Accordingly, the disclosure of Caetano-Annoles is seriously deficient and cannot support a *prima facie* case of obviousness. The Examiner also has not pointed to any permissible source of objective evidence that would cure these deficiencies in Caetano-Annoles. Hence, a *prima facie* case of obviousness has not been established, and reconsideration and withdrawal of the rejection of claims 1, 2, 5-6, 9-15, 23-29 and 66 under 35 U.S.C. § 103(a) are respectfully requested.

V. The Rejection Under 35 U.S.C. § 103(a) Over Caetano-Anolles in view of Huo

In the Office Action at pages 4-5, the Examiner has rejected claims 21 and 22 under 35 U.S.C. § 103(a) as being unpatentable over Caetano-Anolles as applied to claims 1, 2, 5-6, 9-15, 23-29 and 66 in view of Huo (U.S. Patent No. 5,922,535, hereinafter "Huo").

Present claim 21 (and hence, claim 22 that depends ultimately therefrom and that is also rejected) depends ultimately from claim 1. Present claim 1 recites the use of a DNA polymerase mutated to be substantially reduced in the ability to add one or more non-templated nucleotides to the 3' terminus of a DNA molecule. For reasons discussed above, which are reiterated and incorporated herein by reference, Caetano-Anolles is seriously deficient as a primary reference. Huo does not cure this deficiency, as this reference also does not disclose, suggest or otherwise contemplate the use of such a mutated DNA polymerase. Hence, there is no disclosure or suggestion in Caetano-Anolles or Huo that would have motivated one of ordinary skill in the art to have combined their disclosures in an attempt to make and use the presently claimed invention. Absent such suggestion and motivation, these references may not be properly combined. (*See Fine*, 5 USPQ2d at 1598.)

Applicants therefore submit that the Examiner has not met the required burden to establish a *prima facie* case of obviousness. Accordingly, it is respectfully requested that the rejection of claims 21 and 22 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

VI. Provisionally Allowable Subject Matter

In the Office Action at pages 5-6, the Examiner has objected to claims 7-8, 16-20, 30-33, and 69-72 as being dependent upon a rejected base claim. In making this objection, the Examiner also notes that these claims would be allowable if rewritten in independent form including all of the limitations of the rejected base claim. Applicants acknowledge this identification of provisionally allowable subject matter. However, Applicants respectfully traverse this objection, and submit that in view of the forgoing remarks, all of the currently pending claims are allowable. Reconsideration and withdrawal of the objection to these claims are therefore respectfully requested.

VI. Conclusion

All of the stated grounds of rejection and objection have been properly traversed. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and objections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Brian J. Del Buono
Attorney for Applicants
Registration No. 42,473

Date: August 26, 2003

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600
160,906-1